

S. Goldin, et al.  
USSN: Unassigned  
Filed: Herewith  
Page 2

February 3, 1994, now abandoned, the teachings of which are incorporated herein by reference.--.

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IN THE CLAIMS:

- ✓ Page 142, claim 17, lines 3-4, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 143, claim 18, line 3, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 143, claim 19, line 4, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 143, claim 20, line 3, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 143, claim 21, line 4, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 143, claim 22, line 9, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Pages 143-144, claim 23, lines 4-5, please change "claims 1-15" to --claims 1, 8, 11 or 13--;
- ✓ Page 144, claim 24, line 2, please change "claims 1-15" to --claims 1, 8, 11 or 13--.

**REMARKS**

Applicant respectfully requests that the subject Continuation Application be preliminarily amended as provided in the foregoing amendment prior to calculation of the filing fees.

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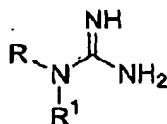
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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1-24. (Canceled)

<sup>1</sup>  
25. (Currently amended) A method for treating a disorder of the nervous system in which the pathophysiology of the disorder involves excessive or inappropriate release of a neurotransmitter from neuronal cells, comprising administering to a mammal exhibiting symptoms of the disorder or susceptible to the disorder an effective amount of a compound of the following formula



wherein R is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, ~~or a substituted or unsubstituted aralkyl having at least about 5 ring atoms,~~ or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, or substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

<sup>2</sup>  
26. (Previously presented) A method of claim <sup>1</sup>25 wherein at least one of R and R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

<sup>3</sup>  
27. (Previously presented) A method of claim <sup>1</sup>25 wherein both R and R<sup>1</sup> are substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

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28. (Canceled)

<sup>4</sup> 29. (Previously presented) A method of claim <sup>1</sup>25 wherein R and R<sup>1</sup> are substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl or substituted or unsubstituted benzyl.

<sup>5</sup> 30. (Previously presented) A method of claim <sup>1</sup>25 wherein the compound is selected from the group consisting of:

N-(4-*sec*-butylphenyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-benzylguanidine;  
N-(3-acenaphthyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(3-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(2-fluorenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(cinnamylmethylene)guanidine;  
N-(4-*n*-butoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-biphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-indanyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-trifluoromethoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(methoxy-1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-chloro-1-naphthyl)-N-(4-*tert*-benzyl)guanidine;  
N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthylmethyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine;

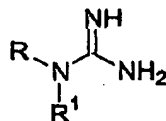
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N-(3-trifluoromethylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-methylthiophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(cinnamyl)guanidine;  
N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine;  
and pharmaceutically acceptable salts thereof.

<sup>6</sup> 31. (Previously presented) A method of any one of claims <sup>1-3, 4, 5, 25-27, 29-30</sup> 25 through 30 wherein the mammal is suffering from a neurodegenerative disorder.

<sup>7</sup> 32. (Previously presented) A method for treating a mammal suffering from or susceptible to a neurodegenerative disease, comprising administering to the mammal an effective amount of a compound of the following formula



wherein R is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

<sup>8</sup> 33. (Previously presented) A method of claim <sup>7</sup> 32 wherein at least one of R and R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

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<sup>9</sup>  
~~34~~ (Previously presented) A method of claim <sup>7</sup>~~22~~ wherein both R and R<sup>1</sup> are substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted alkyl.

35. (Canceled)

<sup>10</sup>  
~~36~~ (Previously presented) A method of claim <sup>7</sup>~~22~~ wherein R and R<sup>1</sup> are substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl or substituted or unsubstituted benzyl.

<sup>11</sup>  
~~37~~ (Previously presented) A method of claim <sup>7</sup>~~22~~ wherein the compound is selected from the group consisting of:

N-(4-*sec*-butylphenyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-benzylguanidine;  
N-(3-acenaphthyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(3-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*isopropylbenzyl*)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(2-fluorenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(cinnamylmethylene)guanidine;  
N-(4-*n*-butoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-liphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-indanyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-trifluoromethoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(methoxy-1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-tolophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-chloro-1-naphthyl)-N-(4-*tert*-benzyl)guanidine;  
N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;

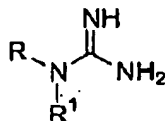
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N-(4-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthylmethyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine;  
N-(3-trifluoromethylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-methylthiophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(cinnamyl)guanidine;  
N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine;  
and pharmaceutically acceptable salts thereof.

<sup>12</sup>  
~~28~~. (Previously presented) A method of any one of claims ~~32-34~~ or ~~36-37~~ <sup>7-9 10-11</sup> wherein the neurodegenerative disease is Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, Alzheimer's disease, Down's Syndrome, Korsakoff's disease, olivopontocerebellar atrophy, HIV-induced dementia or blindness, multi-infarct dementia or diabetic neuropathy.

<sup>13</sup>  
~~30~~. (Previously presented) A method of treating a disease in which the pathophysiology of the disease involves inappropriate cellular secretion comprising administering to a mammal suffering from or susceptible to the disease an effective amount of a compound of the following formula



wherein R is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, or substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring

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members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

<sup>14</sup>  
~~40.~~ (Previously presented) A method of claim <sup>13</sup>~~39~~ wherein at least one of R and R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

<sup>15</sup>  
~~41.~~ (Previously presented) A method of claim <sup>13</sup>~~39~~ wherein both R and R<sup>1</sup> are substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

42. (Canceled)

<sup>16</sup>  
~~43.~~ (Previously presented) A method of claim <sup>13</sup>~~39~~ wherein R and R<sup>1</sup> are substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl or substituted or unsubstituted benzyl.

<sup>17</sup>  
~~44.~~ (Previously presented) A method of claim <sup>13</sup>~~39~~ wherein the compound is selected from the group consisting of:

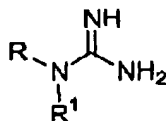
N-(4-*sec*-butylphenyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-benzylguanidine;  
N-(3-acenaphthyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(3-acenaphthyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(2-fluorenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(cinnamylmethylene)guanidine;  
N-(4-*n*-butoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-biphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-indanyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-(1-fluoromethoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;

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N-(3-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(methoxy-1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(3-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(4-chloro-1-naphthyl)-N-(4-*tert*-benzyl)guanidine;  
 N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(4-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(1-naphthylmethyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine;  
 N-(3-trifluoromethylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(3-methylthiophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
 N-(5-acenaphthyl)-N-(3-iodobenzyl)guanidine;  
 N-(5-acenaphthyl)-N-(cinnamyl)guanidine;  
 N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine;  
 N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine;  
 and pharmaceutically acceptable salts thereof.

<sup>18</sup>  
 25. (Previously presented) A method of modulating the release of excess endogenous neurotransmitters from a mammal comprising administering to the mammal an effective amount of a compound of the following formula



wherein R is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, or substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring



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members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

<sup>19</sup>  
~~46.~~ (Previously presented) A method of claim <sup>18</sup>~~45~~ wherein at least one of R and R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted alkyl.

<sup>20</sup>  
~~47.~~ (Previously presented) A method of claim <sup>18</sup>~~45~~ wherein both R and R<sup>1</sup> are substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted alkyl.

48. (Canceled)

<sup>21</sup>  
~~49.~~ (Previously presented) A method of claim <sup>18</sup>~~45~~ wherein R and R<sup>1</sup> are substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl or substituted or unsubstituted benzyl.

<sup>22</sup>  
~~50.~~ (Previously presented) A method of claim <sup>18</sup>~~45~~ wherein the compound is selected from the group consisting of:

N-(4-*sec*-butylphenyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-benzylguanidine;  
N-(3-acenaphthyl)-N-benzylguanidine;  
N-(5-acenaphthyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(3-acenaphthyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*isopropyl*benzyl)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(2-fluorenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(cinnamylmethylene)guanidine;  
N-(4-*n*-butoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-*hiphenyl*)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-indanyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-(trifluoromethoxy)phenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;

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N-(3-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(methoxy-1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-chloro-1-naphthyl)-N-(4-*tert*-benzyl)guanidine;  
N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthylmethyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine;  
N-(3-trifluoromethylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-methylthiophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(cinnamyl)guanidine;  
N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine;  
and pharmaceutically acceptable salts thereof.

51-59. (Canceled)